METABOLISM

In

DEMENTIA PRAECOX

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THE BASAL METABOLIC RATE IN DEMENTIA PRAECOX

General Considerations:-

The subject of basal metabolism is of great interest in connection with the study of mental diseases, but at the present time little or no work has been done on the subject. Dealing with the psychopathology of puberty and adolescence in the Morison lectures of 1921, Sir Frederick Mott refers to the subject of metabolism in Dementia praecox, and states that "it is quite probable that there is a hypofunction of the whole of the bodily tissues, especially of the reproductive and endocrine systems, and associated with deficient oxidation processes."(i) The estimation of the basal metabolic rate in similar cases of mental derangement should throw some light on the point as to whether there is a deficiency in the oxidation processes. According to Voit, "the absorption of oxygen does not cause metabolism, but the amount of metabolism determines the amount of oxygen to be absorbed." It is frequently stated in the literature that a given disease is the consequence of edficienct oxidative power in the tissues. It is not due to lack of oxygen that sugar is not oxidised

in diabetes. There is a normal supply of oxygen present, but the cleavage of the sugars into bodies which can unite with oxygen cannot apparently be effected, and hence they cannot be metabolised.(ii) So far I have been able to find only one reference in the literature to the estimation of the basal metabolic rate in cases of mental disorder; Grafe: Deutsches Archiv. fur klin. Med. 1911, CII, 15. He has analysed 29 cases of stupor, and in the majority found no variation from the usual normal metabolism. In 8 cases, however, there was a metabolism which was between 17 and 39 per cent lower than normal. A considerable percentage of these cases of stupor were in all probability cases of Dementia praecox, although it is common knowledge that a phase of stupor does occur from time to time during the course of many of the other forms of mental disorder, including the definitely organic varieties, such as Dementia paralytica.

Having thus briefly stated what I have been able to obtain from the literature on the subject of basal metabolism in mental disorder, I shall now proceed to relate my own observations, which were concerned almost wholly with cases of Dementia praecox.

Limitations and Precautions:-

There are obviously limitations to metabolism determinations, even in sane people. Wm.S. McCann states, "besides errors due to apparatus, technique, etc. far more subtle sources of error exist within the patient. The obvious ones are muscular movements, surreptitiously taken food, failure to rest for a sufficient time before the test, all of which may be avoided. Mental excitement or agitation plays an important role with many patients in whom it may readily be overlooked."(iii)

Such influences as these are even more pronounced when persons with mental disorder are dealt with. The difficulty of obtaining the patient's co-operation is often very great. It is quite easy to have the patient resting in bed for at least 18 hours without food in a suitable environment conducive to peacefulness of mind and freedom from extraneous noises, as was done as a preliminary to these tests, and yet these precautions will not eliminate such psychical influences as fears, worry, etc., important factors of a purely subjective character, and not revealed to an observer even with the keenest powers of observation. Cannon has clearly demonstrated that emotional excitement produces a

temporary increase of blood sugar [iv] and other bodily changes, associated with an increased outpouring of adrenin, which goes to show that the rate of metabolism must be accelerated as a result of psychical influences. Although it has been possible to estimate the basal rate in several other cases of mental disorder, including melancholia, in which there has been an apparent absence of such psychical disturbing factors, it was soon appreciated that the test was more consistently reliable in cases of Dementia praecox belonging to the hebephrenic type, displaying marked apathy. The only case of Catatonic stupor available could not be utilized, because the muscular rigidity prevented his height and weight from being determined. In the cases of the hebephrenic type referred to, the essential condition of the patient's co-operation was indirectly obtained by the presence of imperception and apathy. The attempt to overcome muscular rigidity, soothe mild restlessness, correct irregular and often accelerated breathing, and calm emotional disturbance as revealed by an accelerated pulse-rate, etc., which is possible in the majority of sane people with patience and practice, was soon realised to be a potent disturbing factor in the proper conduction of the test in

the insane, because negativism and similar states were so easily induced. It was soon observed that the best procedure to eliminate disturbing factors was for the examiner himself as it were to be negativistic prior to and during the test; i.e. to maintain silence and to have patience and plenty of time available, because sooner or later all the cases examined except one passed into a state of complete muscular relaxation with quiet regular breathing, etc. which is so essential for the proper condition of a test, if the result is to be relied upon. Many of the patients examined gave no trouble in this respect, remaining from the onset indifferent and unmindful of the presence of the face-mask, the disturbing influence of which in these was less marked than in sane patients of the nervous type.

The Method employed to determine the Basal Metabolic Rate:-

The Douglas bag method was for several reasons employed in preference to the other available methods of indirect calorimetry, involving the use of a spirometer such as Benedict's apparatus. E.P.Cathcart cites the names of several well-known investigators in this field of work to show that this method possesses unique advantages. He quotes Yandell

Henderson as follows:- "This apparatus is much simpler and easier to use, more accurate, and affords more nearly normal conditions as regards the air breathed by the subject, than any other device with which we are acquainted. It is equally adaptable to all conditions."(v) Further, the absence of a complicated piece of mechanism by the bedside is most advisable when dealing with a mental patient if other disturbing factors are to be avoided. A face-mask, such as that sold by Siebe Gorman and Co. was of necessity used in preference to a mouth-piece, seeing that the latter requires the active and intelligent co-operation of the patient. No trouble was experienced in the use of the face-mask. Haldane's apparatus was used for the analysis of the expired air.

Instead of the usual sampling tube, a 30.c.c. ground-glass syringe was used as described in Macloed's "Physiology," p.561. This modification can be thoroughly recommended. It is simple to use, reliable and free from the manipulative disadvantages of a sampling tube. Apart from the above modifications, the method of procedure followed was that described in Macloed's "Physiology and Biochemistry in Modern Medicine," E.P.Cathcart's article in the Journal of the R.A.M.C., Nov. 1918", and in Haldane's

"Methods of Air Analysis." Each patient had no food for at least 18 hours prior to the test and was resting in bed during that time and until after the collection of the air expired in ten minutes, as determined by a stop-watch. During the collection of the expired air, the pulse and respiratory rates were noted. Immediately afterwards the patient's height and weight were measured.

Definition and Standardization of the Basal Metabolic Rate in normal persons:-

Starling's definition of basal metabolism is as follows:- "The energy output to keep the body alive; i.e. to maintain its warmth and to maintain the energy for respiratory movements, contractions of the heart, etc." Another definition given by H.C.Mosenthal and H.E.Marks is,(vi) "The minimal heat production in the post-absorptive state, that is fourteen or more hours after the taking of food, constitutes an individual's basal metabolism." Both definitions make clear what is meant by basal metabolism, but further amplification is necessary so that a correct interpretation of normal results may be possible after making allowances for several inconstant factors; e.g. general nutrition of the body whether the subject is obese or thin, variations in

height and weight, etc. The determining factor of energy output is undoubtedly the general condition of bodily nutrition - the active mass of protaplasm of the body, (Benedict). Rubner has shown that the heat value of the metabolism of the resting individual is proportionate to the area of the surface of his body. This observation has been confirmed by the experiments of Atwater and Rosa and of Du Bois. Below are given the average results obtained by several observers:-

		Average Calories per sq. metre per hour.	Maximum variation per average per cent.
Average 9 normal controls,	(Du Bois).	39.7	+4 & - 6.
" " " "	(Means).	39.6	+7.6 & - 7.1
" 82 " "	(Benedict).	38.6	Usually ±10.

Lusk. ("Science of Nutrition").

As the results of Du Bois were obtained by calorimeter experiments of two or three hours duration, the figure 39.7 calories per square metre of body surface per hour may be accepted as closely approximating to the normal basal heat production of adult men. Du Bois has evolved a formula to express surface area in

terms of height and weight:-

Surface Area = Weight x 0.045 x Height x 0.725 x 71.84., and also a chart by which the surface area in square metres for various heights in centimetres and weights in kilograms is easily determined.(vii)

Again it has been shown that females have a lower energy output than males, (usually about 6.8% lower).

The Nature of the Cases investigated:-

Amongst the cases submitted to the test were 17 suffering from Dementia praecox, belonging to the hebephrenic group and showing well-marked apathy. The test on the only case of catatonic stupor had to be abandoned, as previously mentioned, because it was impossible to measure his height and weight. However, it is interesting to note that this patient's respiratory quotient was 0.73, a figure having a similar relationship to that generally found in the 17 cases of Dementia praecox. Each of the above patients was tested five times on various occasions during the past twelve months. I append (see Table (2)) the results of two examinations of four other patients, two suffering from imbecility, one from manic depressive insanity in remission, and the last from recent malancholia. I do not intend to make any deductions from the results obtained in the

four other cases of mental disorder, beyond alluding to the fact that in all the tests the results were within the normal limits as laid down by Benedict, Lusk, etc. - previously referred to - for normal healthy individuals, and also that the respiratory quotient is decidedly higher than that obtained in the cases of Dementia praecox examined.

The data derived from the examination of the cases of Dementia praecox, considered under the headings of the tables appended:-

Age and sex: The normal basal rate varies according to age, decreasing gradually from youth to old age. The rate for females is about 6.8% lower at corresponding ages. The following is a table of normal rates according to age and sex:-

Age	Male	Female
18-20	41.0	38.0
20-30	39.5	37.0
30-40	39.5	36.5
40-50	38.5	36.0

The percentage deviation in the cases examined has been determined in relation to the above normal rates.

Pulse and Respiration: In four cases, viz., cases 6, 10, 11, 12, acceleration in one or both these rates appear to have had an influence in increasing the

basal rate. Cases 10, 11, 12 demonstrate how an increased respiratory rate causes a greater output of expired air in a given time, and consequently a higher basal rate. In only one case, viz., case 10, has muscular rigidity with negativism been present in addition to increased respiration leading to a still higher basal rate. If due allowance were made for these exciting factors the basal rate must be lower considerably, if not to within normal limits. Generally speaking it has been observed that the variation in the basal rate has resulted more from the variation of the total amount of expired air than from any of the other factors which can have an influence, except possibly that of body weight, the latter being in all cases lower than what is normally found in persons of similar height and stature.

Body Weight:- In only one case (Case 6) was there a marked decrease of body weight. This patient had the lowest calorie-expenditure per hour, and yet the basal metabolism was above the normal rate. This shows that a body with a small area requires less heat to be expended for its basal requirements. Such a case is an excellent example of the necessity for expressing rates in terms of constant, such as per square

square metre of body surface per hour according to the formula of Du Bois for purposes of comparison.

The Volume of Expired Air per hour at the constant: N.T.P. i.e. 0°.C., and 760 m.m.: A variation in this amount is shown to have a potent influence in increasing or diminishing the basal metabolic rate. A higher metabolic rate has always been found associated with a greater volume of expired air, and vice versa. Differences in the respiratory rate and depth of a respiration probably account for this association which emphasises the importance of getting the patient to breathe as he would do in ordinary circumstances. Of course it is important to take into consideration that the character of the respiratory movements varies enormously, especially in cases of Dementia praecox. In this connection it is worthy of note that in all of the cases of Dementia praecox the volume of expired air per hour was very much lower than that found in normal healthy individuals and in the cases of mental disorder other than those of this type. Recalling the fact that metabolism controls the intake of oxygen into the body, and consequently the respiratory movements, it follows that in Dementia praecox there is either a smaller demand by the tissues

for oxygen or a diminished, possibly an impaired absorption of oxygen.

The Respiratory Quotient:-

This is the ratio of the volume of carbon-dioxide exhaled to that of oxygen retained by the body in a given time, and in health is on the average about 0.85. In man and the higher mammalia the only condition apart from diet which can affect the nature of the combustion process is disease. (Macloed).(viii) The exact significance of a lowered respiratory quotient is still under dispute, but it should be noted that in the Dementia praecox cases examined a rate lower than the average normal rate was found. This observation is in harmony with that above-mentioned, regarding the volume of expired air.

The Basal Metabolic Rate:-

A normal range of $\pm$ 10% is allowed by investigators like Benedict, Joslin, Allen,and Du Bois, although several other authors consider that the greater range of $\pm$ 15% is within normal limits. Taking the normal range to be within $\pm$ 10%, ten out of the seventeen cases of Dementia praecox must be considered as having a normal basal metabolism, the remaining seven cases with the exception of two having a subnormal rate. Cases 10 and 11 are the

exceptions, because the increased rate recorded is disregarded for purposes of comparison for reasons already given, as disturbing factors were known to be present. These cases demonstrate, however, what is to be expected in varying states of restlessness and muscular activity, etc.

On examining the five cases with the sub-normal basal rate - comprising 3 males and 2 females - it is to be noted that the deviation from the normal rate is not excessive, varying from -11 to -28 per cent. They belonged to that type of case with symptoms of mental inhibition, lowered arterial tension and cyanosis of the extremities. These figures furnish decisive evidence that hyperthyroidism is not a feature in Dementia praecox, at any rate in the cases here examined. Otherwise the conclusions are more or less in harmony with the findings of Grafe, previously referred to, and is not quite unexpected, because the organism appears to be able to adjust within limits its economy in such a way that its basal requirements are satisfied, whether the oxidation processes are diminished or not.

Calories expended per hour per Kilo. of Body Weight:

No great variation from the normal rate of 1 calorie per Kilo. per hour for a normal man of

70 Kilos. weight has been found, when the varying weights of the cases are considered in relation to this standard. This rate appears to vary directly with the basal metabolic rate.

Total energy expended in 24 hours:

In all cases where the basal rate is lowered there is a corresponding diminution of daily expenditure of energy. This relationship appears to be constant except where there is present a marked diminution of body weight. For example, case 6 shows a very low daily expenditure with a basal rate above the normal at the same age.

The results found in cases other than Dementia Praecox:

Interest in these results is enhanced by the fact that in every case the data in each column fall within the normal limits found in healthy people. They form a useful control to the cases of Dementia praecox examined, not only for purposes of comparison, but mainly as regards the manner in which the tests have been carried out, including the technique employed.

Conclusions:-

1. In 67% of the cases of Dementia praecox examined, there has been no variation from the usual normal basal

metabolism. The basal metabolism of the remainder was below the normal limits, and all of these cases showed symptoms of mental inhibition.

2. The respiratory quotient was in all cases below the average for healthy persons.

3. There is either a small demand by the tissues for oxygen or a diminished, possibly impaired, absorption.

4. Hyperthyroidism is not a feature in Dementia praecox.

5. In the cases other than Dementia praecox the variations did not exceed those found in normal individuals.

REFERENCES.

(i) "Journal of Mental Science," July, 1921.

(ii) Lusk, "Science of Nutrition," 3rd Edition.

(iii) "The Medical Clinics of North America," March 1921.

(iv) "Bodily Changes in Fear, etc." - Cannon.

(v) E.P.Cathcart, "Estimating Energy expenditure by indirect Calorimetry," R.A.M.C.Journal, November 1918.

(vi) "The Medical Clinics of North America," March 1921.

(vii) "Archiv Int. Med." XVII. p.863. 1916.

(viii) "Physiology and Biochemistry," - Macleod.

Dementia Praecox.

Table 1.

Basal Metabolic Rate.
Average of 5 estimations.

Name & Sex	Age	Pulse	Respirations	Body weight in Kilograms.	Gaseous exchange for hour at N.T.P. in litres	Respiratory Quotient.	Calories per hour per Body weight.	Basal Metabolic Rate	% above or below normal for same age	Calories per hour per Kilo Body weight	Total Energy expended in 24 hours	Normal Basal rate for same age.
Females:												
1) D.W.	22	66	16	50·1	218·59	·74	49·7	32·9	-12	0·96	1177	37·0
2) W.O'G.	27	67	16	47·3	233·99	·74	52·14	38·3	+3	1·1	1233	37·0
3) G.C.T.	35	68	15	57·0	210·48	·73	50·45	32·5	-11	0·9	1183	36·5
4) S.T.	28	71	16	58·5	253·93	·74	62·38	39·6	+7	1·0	1445	37·0
5) E.D.	20	62	15	51·0	249·49	·73	63·67	36·2	-3	1·0	1312	37·0
6) E.H.	40	89	17	38·9	215·07	·71	49·0	39·0	+8	1·2	1138	36·0
Males:												
7) C.J.	29	60	14	56·0	200·13	·75	47·02	28·7	-28	0·84	1098	39·5
8) L.R.J.	23	74	16	61·7	290·20	·74	70·12	37·6	-5	1·0	1563	39·5
9) W.G.N.	33	71	15	49·0	221·79	·73	50·45	32·6	-18	0·9	1183	39·5
10) C.H.	32	78	19	52·1	342·81	·74	77·91	50·6	+28	1·4	1843	39·5
11) H.C.	39	71	19	55·1	303·67	·73	73·91	47·0	+17	1·2	1755	39·5
12) C.H.	18	84	18	54·9	301·89	·74	71·31	43·0	+4	1·2	1680	41·0
13) J.B.	21	76	15	62·6	312·52	·76	70·4	42·9	+7	1·1	1664	39·5
14) J.R.O.B.	19	77	17	60·5	336·4	·73	77·0	44·0	+7	1·2	1824	41·0
15) C.C.	25	69	12	58·6	275·48	·73	65·3	40·8	+2	1·0	1574	39·5
16) K.J.	23	62	15	70·2	256·99	·76	58·3	31·0	-22	0·8	1381	39·5
17) C.M.S.	24	65	16	57·7	348·31	·73	69·8	43·6	+10	1·1	1614	39·5

Dementia Praecox.

Table 11.

Basal Metabolism in the cases belonging to other types of the Psychoses.

Name & Sex	Age	Pulse.	Respiration	Body weight in kilograms	Rate of expiration for hour at N.T.P. in litres	Respiratory Quotient	Calories for hour for Body weight	Basal Metabolic Rate	% above or below normal for same age.	Calories for hour for kilo Body weight	Total energy expended in 24 hours	Normal Basal rate for same age.
18). Females:- Imbecility	M.A.P. 25	74	16	58.0	285.90	.85	56.8	36.6	−2	0.9	1353	37.0
		71	15	55.0	227.34	.75	50.8	34.2	−8	0.9	1213	"
19). A.S.: Manic-depressive in remission.	30	72	16	50.0	256.32	.87	52.4	33.6	−8	1.0	1258	36.5
		72	16	58.0	282.78	.77	55.1	36.1	−1	1.0	1323	
20) V.S. Imbecility	36	72	16	49.0	240.84	.73	48.6	34.2	−7	0.9	1166	36.5
Male:- 21). R.J.L. Melancholia	42	76	16	73.0	366.18	.89	71.9	39.06	+1	0.9	1725	38.5
		72	16	73.4	311.20	.75	71.8	38.4	−1	0.9	1725	"

THE REACTION OF THE URINE IN 120 CASES OF MENTAL DISORDER

General considerations:

Two methods are available to determine the reaction of a fluid. The first is the method of titration for acidity or alkalinity in which a standard solution of acid or alkali is added until a certain change in the colour of a suitable indicator is detected. The second method is to determine the hydrogen-ion concentration present in the fluid. The latter is the only satisfactory method of measuring the reaction of a fluid. The hydrogen-ion concentration expresses the reaction of neutral, acid and alkaline solutions. The electrical is the standard method, but for clinical purposes is too intricate. The colorimetric method is less complicated. It is based upon the fact that each indicator has a characteristic zone of hydrogen-ion concentrations within which its colour-changes occur. For details as to the theory and technique of this method, the reader may be referred to Clarke and Lubs, (J.Bacteriol. 1917. ii) and Cole, (Practical Physiol. Chem. pp.19 - 30).

In this investigation of the commoner forms of mental disorder two main objects have been in view. Firstly, to determine the hydrogen-ion concentration at fixed hours during the day to find out how this may vary and whether anything characteristic occurs. Secondly, if a high concentration pointing in the direction of the possible presence of acidosis is related to a corresponding depletion of the alkaline reserves of the body.

Procedure adopted:

Specimens of urine were collected at 7 a.m., 2 p.m., and 6 p.m., in vessels specially provided. As a precautionary measure to prevent contamination written directions were supplied to the wards. The colorimetric determinations were carried out immediately each batch of urines was obtained at the stated times. Too much importance cannot be attached to the immediate examination of organic products like urine which so readily decompose. A second series of three specimens from each patient was examined in the same manner.

Analysis of the results obtained:

Macleod states that in health the Ph., i.e., the hydrogen-ion concentration, varies from 0.000016N

(Ph = 4.8) to about 0.000-000035N (Ph = 7.46) with a mean of about 0.000001N (Ph = 6). These extremes are rarely overstepped in disease, but frequently the average is considerably different. The reaction of the urine in this series of cases showed a similar variation, the highest reading obtained being Ph.4.9 and the lowest Ph.6.9 (Sorensen's logarithmic method for expressing the hydrogen-ion concentration, i.e. the smaller the Ph number the greater the degree of acidity and vice versa). In the majority of the cases the reaction of the urine varied during the course of the day, but not excessively, the change being in the direction from a lesser to a greater degree of acidity, e.g. 7 a.m. Ph.6.1; 2 p.m. Ph.5.7; 6 p.m. Ph.5.8. Amongst the cases showing little or no variation during the day were several including 77% of the cases of Dementia praecox, the reaction of which was decidedly acid. Recalling that in disease the limits of physiological variation are rarely overstepped, for example in cardio-renal disease, the mean acidity may be approximately Ph.5.3 or five times the normal average value, it was reasonable to assume that probably acidosis was present when the Ph was 5.4 to 4.8.

Was there any relation between the apparent acidosis found in the few cases above referred to and the alkaline reserves of the body?

The estimation of the hydrogen-ion concentration is insufficient in itself to warrant a diagnosis of acidosis. Palmer and Henderson (2) recommend the colorimetric determination of the hydrogen-ion concentration of the urine as a control to A.W. Sellard's test, i.e. "The tolerance to alkali test." In the present instance the hydrogen-ion method was used for sorting out purposes, so to speak, and the alkali tolerance test determined in those cases with a markedly acid reaction. In other words, irrespective of the order in which the tests are done, a positive result in both is essential. A.W.Sellard's (3) states that the increase in the tolerance to bicarbonate is the most delicate of the tests which are specific for acidosis. By the use of this test it was possible to detect very slight grades of experimental acidosis. He defines acidosis as essentially an impoverishment of the blood and other tissues in fixed bases or in substances which readily give rise to fixed bases. Death takes place before any significant change occurs in the reaction of the blood. Henderson states that the constancy of the

blood's reaction at Ph 7.45 is even more carefully guarded than the other great constants of the body.

The Method employed in the alkaline tolerance test:

1. The patient is in bed and emptied the bladder at 10 a.m.
2. Immediately afterwards 4 grams of sodium bi-carbonate in a little water is taken by the mouth.
3. At 11 a.m., 12 p.m., 1 p.m., the bladder is emptied and each specimen tested for the degree of acidity present.
4. The degree of acidity is determined by two methods:-
   (a) By titration against N/50 NAOH using phen-olpthalein as indicator.
   (b) By the colorimetric determination of the hydrogen-ion concentration.

It was more difficult to be exact with the titration method, only a small quantity of urine being available in some cases, although it was useful as a control to the other method.

Interpretation of results:

W.W.Palmer and L.J.Henderson suggest that a condition of acidosis may be assumed to exist when the administration of a quantity of alkali equivalent

to one litre of N/10 solution fails to produce a diminution in the acidity of the urine. Four grams of sodium bicarbonate makes approximately 500 c.c. of N/10 solution.

The following table shows the nature of the results:-

Case.	Hydrogen-ion conc.				Acidity as percentage of normal acid.	
	10am	11am	12pm	1pm	10am	12pm
L.R.J.	5.5	7.4	7.6	8.2	1.4	0.3
H.C.	5.8	5.9	7.4	8.1	0.76	0.12
G.L.F.	5.5	7.9	8.3	8.0	0.54	0.24
S.T.	5.1	5.1	-	6.2	1.12	0.9
S.T.	5.0	5.1	menstruat.		4.78	4.28
K.J.	5.8	7.8	8.0	-	2.86	0.2

Seventeen out of the eighteen cases examined showed a diminution in the acidity of the urine in a manner similar to that shown in the above and this table. Diminution is the result normally found after the ingestion of alkali.

The results of the alkali tolerance tests are shown graphically at the end. The sharp upward rise in the curve shows the decided response, which is what one would expect in health. There is therefore no diminution of the alkali reserves in dementia praecox, at any rate in the cases examined.

Conclusions:-

1. The reaction of the urine in the cases of mental disorder examined varied within physiological limits.

2. Those showing a greater degree of acidity were mostly cases of dementia praecox. All except one case behaved normally in the alkali tolerance test.

3. There appears, therefore, to be no depletion of the alkaline reserves of the blood and tissues in the cases of mental disease examined; acidosis is absent.

References:-

1. Arch. Int. Med. Vol.12. p.153.

2. Ditto. Ditto. (clinical studies of acid base equilibrium and the nature of acidosis)

3. The principles of acidosis and clinical methods for its study. A.W.Sellards.

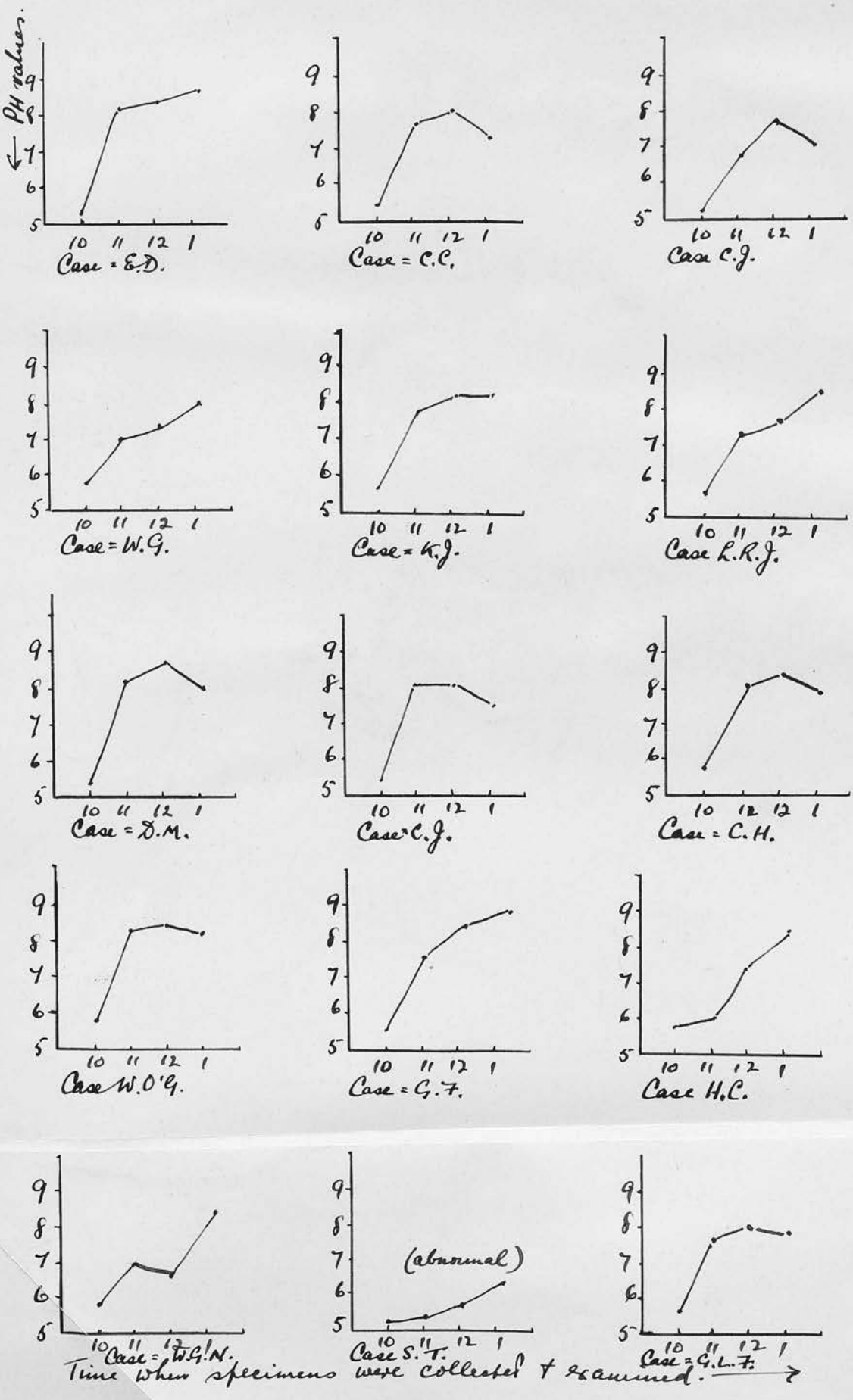
4. Other books referred to:-

(a) Practical Physiological Chemistry - S.W.Cole

(b) Physiological Biochemistry - Macloed.

(c) Journal of Bacteriology, Vol.2 - Clark & Lubs.

The alkali tolerance tests in cases of dementia praecox. The Ph value in the urine at hourly intervals is estimated after the ingestion of 4 grams of Sod. Bicarb.



THE SIGNIFICANCE OF UREA IN DEMENTIA : PRAECOX AND OTHER MENTAL STATES :

Urea is the compound in which the greater part of the nitrogen from protein metabolism is normally excreted, and of which it forms an important index.

Before the urea content of the urine can be of use for this purpose it is necessary that the efficiency of the kidneys should be determined, for it is recognised that patients with defective kidneys are incapable of passing urine with a high concentration of urea. Evidence of kidney disease other than the percentage of urea in the urine being negative, there are many causes for a low percentage such as a diminished protein diet, vascular changes, and a reduction in the resistance to filtration through the kidney tubules.

Method employed to eliminate Renal Disease.

The patient is submitted to a clinical examination, particular attention being directed to the symptoms and signs pointing to renal disease.

The concentration tests, described by

Maclean in the Lancet dated the 19th June 1920, are now employed. These consist of the following. Three and a half hours after a breakfast consisting of bread butter and tea, the patient is directed to empty the bladder and then to drink 15 grams of urea dissolved in 200 cc of distilled water. At the end of an hour the patient empties his bladder, and again after another hour's interval. The respective specimens are collected in specially labelled bottles. The analysis is proceeded with immediately afterwards. The volume of urine excreted at each of the respective hours is measured in cubic centimetres. The percentage urea concentration is estimated by Maclean's modification of the hypobromite method, where 8 cc of nitrogen are taken as equivalent to 0.5% of urea. This estimation is done in the second hour specimen.

On the day prior to the above, 10 cc of blood are collected by venu-puncture in a test-tube containing oxalate crystals to prevent clotting, and was done at the same time of day. The technique advised by Maclean for the analysis was employed, and this was done soon after the specimen was obtained. The average of two estimations was taken as the measure of the percentage concentration of urea in the blood. A separate specimen of urine was examined microscopically for casts. Albumen was tested for by

the heat and salicylic-sulphonic reagents.

The results of these tests.

These are set out in Table 1. The upper percentage amount of urea in the blood in health is given by Maclean as 40 mg. Other observers have placed this limit at a lower level. All of the 28 cases of dementia praecox examined have a concentration within the above limits, which are compatible with efficiently working kidneys. The results vary from 9 mg per cent upwards. It is worthy of note in this connection that most of the cases having the higher concentration in the blood had a correspondingly increased percentage in the urine, and the converse held good also in the majority with the low concentration. The results obtained in the percentage urea concentration in the urine are interesting, although apparently anomalous. The lowest percentage amount given which is compatible with healthy renal activity is 2. Of the cases of dementia praecox 57% had a lesser concentration than this. In none of these cases was the other available evidence in favour of renal disease. Diureris, although present in the majority, was also found in some of the other cases. This factor was present in 32% of the total number of cases of dementia praecox, and it appears to be in

part due to the same cause as the low urea percentage. This observation was almost entirely absent in 55 cases belonging to other forms of mental disorder. From all the evidence it appears reasonable to assume that there was no kidney disease in any of the cases of dementia praecox examined.

Casts and albumin were not found in any of the cases.

An examination of 24 hour specimens of urine.

Each patient received the following diet, viz. 2 pints of milk, 2 eggs, milk pudding, bread and butter, and fluid in any other form excluded. He was confined to bed for two days prior to and during the collection of the specimen.

The following estimations were made, the total quantity of urine excreted during the 24 hours, the total acidity in terms of N/10 acid, the total amount of urea excreted and its percentage, the total excretion of ammonia. The urea and ammonia having been converted into grams of nitrogen their ratio was calculated. Urea was estimated by the Hypobromite method previously mentioned, and the acidity and ammonia by Folin's Formalin method using phenolphthalein as the indicator.

The results obtained.

These are set out in Table III. The percentage amounts of urea in the blood and urine from the concentration tests are included to facilitate comparison.

Urea.

There is a corresponding low urea percentage in almost all the cases who had a similar amount in the concentration tests. Although the total amount of urea excreted daily is subject to wide variation in health, the average of 2% is taken as representing the lower limit found in healthy individuals. The total daily excretion of urea is given as between 25 and 40 grams. In 15% of the cases the daily amount excreted was above 25 grams, and this was more or less in harmony with the percentages found in the concentration tests and daily specimens. The remaining 85% of the cases showed a daily excretion below this figure, the average being in the neighbourhood of 15 grams.

Ammonia.

Ordinarily the daily output of ammonia expressed as nitrogen does not exceed 0.5 to 0.6 gram. In 74% of the cases of dementia praecox the amount

of ammonia nitrogen was greater than 0.6 reaching in a few instances as high as 1.0 gram.

The Urea-nitrogen ammonia-nitrogen ratio.

In health it is recognised that the urea-nitrogen is 16 and more times that of ammonia-nitrogen. 84% of the cases showed a lowered ratio ranging between 15 and 10. The smaller the number the greater is the degree of pathological change. In any case a varying degree of abnormality is indicated in the cases examined, the significance of which will be considered later.

Quantity of urine excreted daily.

As with the urea so is the daily amount of urine excreted subject to variations in health, but from 1000 to 1800 cc are reckoned as the average amount under ordinary conditions. The amounts excreted by the cases of dementia praecox are within the above limits, although there is a tendency in the majority towards excessive excretion, and this was more particularly marked the longer the period of chronicity of the cases. As a comparison in this connection the daily excretion of urine was measured under the same conditions in a number of recent cases of other types of mental disorder. The total

amount excreted in the 24 hours was much lower, the average difference being between 20 and 30%.

Interpretation of the results.

Renal disease was absent in all of the 28 cases of dementia praecox. Cases belonging to various types of mental disorder have similarly been investigated and in only 4% of them could it be reasonably decided that renal disease was present (see Table II). As regards dementia praecox it appears reasonable to assume that this type of mental disorder has no relation to renal disease.

The clinical examination of the patients showed that arterial tension was subnormal in the majority of the cases with a low urea percentage in the urine (see Table I). This diminution of tonus, in all probability the consequence of some endocrine disturbance, seems to offer a reasonable explanation not only for the low percentage amount of urea but also for the tendency to polyuria.

A lowering of the urea-nitrogen ammonia-nitrogen ratio is held by some authorities to be indicative of a state of "acidosis" in the tissues. The explanation for this view is that an increased production of ammonia is required to neutralise an excessive amount of acid radicles in the body. The more

generally accepted definition is that acidosis is essentially an impoverishment of the body in alkalies, i.e. an impoverishment of the blood and other tissues in fixed bases or in substances which readily give rise to fixed bases. In the paper on the reaction of the urine in terms of hydrogen-ion concentration it has been shown that there is no real depletion of the alkaline reserves of the body, although there is a tendency in the cases of dementia praecox examined for the PH. value to indicate elimination of acid radicles. Again the analyses show that the abnormal ratio between the two forms of nitrogen is due not only to an increased production of ammonia but also to a diminution of the total output of urea. It is therefore more reasonable to assume that a general slowing of metabolic processes, including that of oxidation, is the cause, and that acidosis in the more accepted definition of the term is absent.

Conclusions.

1. No causative relationship existed between renal disease and dementia praecox in the cases examined.
2. The subnormal percentage of urea is in part at least the result of diminished arterial tone.
3. The abnormal urea-nitrogen ammonia-nitrogen ratio is not an indication of a state of acidosis, but in

all probability the consequence of diminished metabolic processes, including internal oxidations.

References

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2. "Practical Physiological Chemistry" - Cole.

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4. "Dementia Praecox" - Kraepelin, translated by R. M. Barclay.

5. "Acid Base Equilibrium and Acidosis" - Palmer and Henderson, Arch. Int. Med. 1913 Vol. XII. No. 2.

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Table 1.

Dementia Praecox.

Urea concentration tests etc.

Name.	Age & Sex.	1st Hour 2 Hour	Percentage Urea in 2nd Hour.	Spec. Grav. Reac.	Albumin	Percentage Urea in Blood	Systolic Blood Pressure.	Remarks.	Mental Type.
E.S.	30 F.	150cc 70 cc	2·65	1027 N	0	17	118	Nutrition good.	Hebephrenia.
C.J.	44 F.	85 " 100 "	2·09	1018 A	0	24	110	Nutrition good.	Hebephrenia.
E.H.	35 F.	70 " 30 "	1·6	1020 A	0	9	118	Nutrition good.	Catatonia.
W.G.	26 F.	285 " 130 "	1·2	1010 A	0	14	110	Nutrition good.	catatonia.
W.G.N	32 M.	150 " 135 "	1·21	1021 A	0	10	112	Nutrition fair.	catatonia.
S.Y.	27 F.	75 " 40 "	2·5	1018 A	0	18	130	Nutrition fair.	Hebephrenia.
S.M.	21 F.	85 " 65 "	3·03	1016 A	0	18	120	Nutrition fair.	Hebephrenia.
C.D.M.	29 F.	145 " 145 "	1·93	1018 A	0	24	110	Nutrition fair.	Catatonia.
C.J.	28 M	— " 135 "	1·68	1015 A	0	37	108	Nutrition fair.	Hebephrenia.
C.H.	17 M	285 " 80 "	1·93	1018 A	0	39	186	Nutrition good.	Hebephrenia.
M.B.	39 F.	325 " 115 "	1·7	1015 Alk	0	35	86	Nutrition moderate	Hebephrenia.
T.R.R.	26 M	600 " 475 "	1·5	1010 Alk	0	23	112	Nutrition good.	Hebephrenia.
R.M.	33 M	56 " 68 "	4·1	1020 N	0	39	114	Nutrition moderate.	Catatonia.
C.G.	28 M	415 " 160 "	1·5	1016 A	0	15	114	Nutrition good.	Hebephrenia.
C.C.	24 M	485 " 125 "	1·7	1015 Alk	0	17	118	Nutrition good.	Hebephrenia.
E.P									

Table 11.

The concentration tests.

Results summarised according to the type of Mental Disorder.

Mental Disorder.	Number of Cases examined	Blood urea below 40%. & urine above 2%	Blood urea below 40%.	Urine urea above 2%	Urine urea below 2% with diuresis.
Dementia Praec.	28	12	28	12	16
G.P.I.	3	3	3	3	0
Ins with Epilepsy	7	5	7	5	0
Melancholia	19	15	17	14	1
Mania	12	9	11	8	1
Confused States	14	11	10	10	4
Totals.	83	55	76	53	22

Table III.

Dementia Praecox.

The results in the 24 hours specimens of urine.

Name	Age & Sex	Percentages: Urine	Percentages: Blood	Daily quantity of urine	Total Acidity as N/10 Acid	Total Urea grams.	Total urea as grams Nitrogen	Total Ammonia in grams.	Total Ammonia as grams nitrogen	Urea Nitrogen / Ammonia Nitrogen ratio	Percentage urea daily.
C.C.	44m	1·7	17	1000cc	95·8	17·5	8·16	0·964	0·793	10	1·7.
S.M.	21 ♀	3·03	18	1350cc	101·2	17·6	8·26	0·825	0·687	12	1·31.
C.J.	25m	1·68	37	1230cc	196·8	18·4	8·05	0·702	0·578	14	1·5.
L.R.J.	22m	2·6	25	1140cc	387·4	29·5	13·76	1·425	1·17	11	2·59
J.B.	21m	1·8	38	690cc	402·9	27·5	12·83	0·830	0·68	15	4·0
C.H.	17m	1·93	39	1560cc	93·6	18·8	8·77	0·912	0·751	10	1·21
T.R.R.	26m	1·3	23	1620cc	105·7	20·2	9·44	0·8	0·81	11	1·25
E.G.L.	29m	4·5	18	1590cc	298·9	24·8	11·57	1·254	1·03	10	1·56
E.G.	24 ♀	1·92	16	1260cc	1838	29·10	13·58	0·976	0·803	16	2·31
A.P.	21m	5·37	30	510cc	71·4	11·27	5·18	0·291	0·239	11	2·21
M.H.	28 ♀	2·06	39	600cc	309·6	16·54	7·71	0·525	0·432	17	3·09
K.H.	26 ♀	2·87	10	1465cc	134·7	21·64	10·09	0·988	0·813	12	1·93
A.P.	27m	1·81	33	1274cc	97·3	19·33	9·02	0·792	0·652	13	2·10
W.G.M.	32m	1·21	10	1265cc	132·8	21·53	10·05	0·976	0·811	12	1·88
S.T.	27 ♀	2·5	18	1184cc	162·3	16·5	7·70	0·652	0·538	14	2·20
A.S.	30 ♀	1·42	11	1567cc	221·7	23·9	11·10	0·998	0·821	13	1·87
M.B.	33 ♀	2·25	10	1468cc	209·6	21·)	10·10	0·912	0·751	13	1·99
K.J.	23m	1·01	36	1396cc	213·2	18·6	8·68	0·821	0·676	12	1·84
W.G.	26 ♀	1·2	14	1643cc	215·7	17·42	8·12	0·846	0·696	11	1·78